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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,406	FRANCISCO ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11,13-19 and 67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11,13-19 and 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt of the amendment, IDS, affidavits under 37 CFR § 1.132 of Dr. Tsai and Dr. Wahl filed on 7/20/2005 is acknowledged. Claims 1-8, 11, 13-9, and 67 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office action contains new grounds of rejection.

Specification, Withdrawn

The objection of the specification due to an embedded hyperlink and/or other form of browser-executable code is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 112, Withdrawn

The rejection of claims 8, and 13-19 under 35 U.S.C. 112, first paragraph, due to biological material is withdrawn in view of the biological statement provided on pages 8, and 9 of the amendment filed on 7/20/2005, and also by Dr. Tsai statement under 37 CFR § 1.132.

Claim Rejections - 35 USC § 103, Withdrawn

The rejection of claims 1, 2, 5, 7-13, 16, 19, and 67 under 35 U.S.C. 103(a) as being unpatentable over Pohl et al., of record (1993, Int. J. Cancer, vol. 54, pages 418-425) is withdrawn because applicant's argument that the antibodies disclosed in the prior art do not exert cytostatic or cytotoxic effect on a Hodgkin's disease cell line cells in the absence of cells other than cells of a Hodgkin's disease cell line cells.

The rejection of claims 1, 3, 8, 11, 14, 16, and 18 under **35 U.S.C. 103(a)** as being unpatentable over Pohl et al., (cited above), and further in view of Barth et al., of record (June 2000, Blood, vol. 95, page 3909-14) is also withdrawn since Pohl et al., reference is not an art.

The rejection of claims 1, 4, 6, 8, 11, 15, 17 **under 35 U.S.C. 103(a)** as being unpatentable over Pohl et al., (cited above), in view of Barth et al (June 2000, Blood, vol. 95, page 3909-14), and further in view of da Costa et al., of record, 2000, Cancer Chemother Pharmacot, 46(suppl):S33-S36 is also withdrawn since Pohl et al., reference is not an art.

The Following Are New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claims 8, 11, 13, 14, 15, 16, 17, 18, and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibody competing for binding of CD30 receptor with AC10 or HeFi-1, does not reasonably provide enablement for any other protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is Aundue≅ include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working

examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 8, 11, 13, 14, 15, 16, 17, 18, and 19 are drawn to method of treating Hodgkin's disease using a protein competing for CD 30 receptor with AC10 or HeFi-1 (base claim 8), or using a protein having at least 95% identity to SEQ ID NO:2 and immunospecifically binds CD30 (base claim 11), wherein the proteins in both claim 8, and 11 have cytotoxic effect on Hodgkin's disease cell line cells in the absence of other effector cells.

The specification discloses that AC10 and HeFi-1 antibodies binding to CD30 receptor shrinks Hodgkin's tumor in an in vivo model mouse. However, the specification does not teach a structure of any other protein competing for CD 30 receptor binding with AC10 or HeFi-1 and the recited function. One of skill could make and screen an anti-CD30 antibody with the recited function but the claims are broader than an anti-CD antibody because both base claims 8 and 11 recite "protein", which includes natural and unnatural ligands that might be discovered later. Tian et al., (cited below) at page 5335 (see the introduction) teach that a ligand (i.e. CD30L) competing for HeFi-1 is known. However, the ligand does not have the function recited in the claim since Falini et al (cited below) at pages 2-4 under the heading "FUNCTIONS OF THE CD30/CD30L SYSTEM" teach that CD30L enhances the proliferation of the HD-derived cell lines of HDLM2 and L-540 instead of having cytotoxic or cytostatic effect. The instant specification does not teach only anti-CD30 antibodies. It is noted that law requires that

the disclosure of an application shall inform those skilled in the art how to make the alleged discovery, not how to screen it for themselves.

As for claim 11, drawn to method using SEQ ID NO: 2, Voet et al., (1990, Biochemistry, John Wiley & Sons, page 1099-1101 only) teach that the antigen-binding site of an antibody is located between light chain and heavy chain. US Pat. 5,789,554 teachess that an antibody is a protein made up of a string of amino acids, and the antigen binding site is made up of six different stretches of CDRs, both in light and heavy chains (see the boxed in Fig. 1). As the previously provided sequence alignment shows, SEQ ID NO: 2, which is a mouse kappa light chain, does not contain all the necessary binding moiety, therefore would not be able to bind CD30.

Considering the unpredictable state of art, limited guidance, no examples in the except the monoclonal antibodies comprising both light chains and heavy chains, broad breath of the claims, it is concluded that undue experimentation is required to practice the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

Claims 11, 13, 14, 15, 16, 17, 18, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Falini et al., 1995, Blood, vol. 85, pages 1-14.

Claims 11, 14, 15, 16, 17, 18, and 19 are drawn to method of method of Hodgkin's disease treatment by administering a protein comprising an amino acid sequence at least 95 % identity to SEQ ID NO: 2, and immunospecifically binds CD30, and exerts a cytostatic or cytotoxic effects on a Hodgkin's disease cell line in the

absence of cells other than cells of said Hodgkin's disease cell line cells, wherein method further comprises chemotherapy in claims 14, 17, and 18, and wherein said protein is a chimeric antibody in clam 13, conjugated to a cytotoxic agent in claim 15, and s a fusion protein comprising the amino acid sequence of a second protein in claim 16, wherein claim 19 specifies how the cytotoxic effect is determined.

Falini et al., teach method of method of Hodgkin's disease treatment by administering a protein (i.e. anti-CD 30 antibody conjugated to ricin, see the title) which immunospecifically binds CD30, and exerts a cytostatic or cytotoxic effects on a Hodgkin's disease cell line in the absence of cells other than cells of said Hodgkin's disease cell line cells, wherein the method further comprises chemotherapy (note the paragraph bridging pages 9 and 10). The instant claims as currently construed do not exclude a protein with a cytotoxic agent attached to it in order to have the required cytotoxic effect. Note the recited instant SEQ ID NO:2 is a mouse kappa chain (a light chain), which does not bind any antigen, let alone having any cytotoxic effect.

As for at least 95 % identity to instant SEQ ID NO:2 in the instant claim 11, as discussed during the prosecution history, for example, in the Office action mailed on 04/03/2003, any murine antibody, even without CD30 binding capacity inherently comprises a protein comprising at least 95 % identity to instant SEQ ID NO:2. Note the previously provided sequence alignment (with the Office action mailed on 04/03/2003) that the instant SEQ ID NO:2 has about 98 % sequence identity to any mouse immunoglobulins light chain that does not bind to CD30. Thus, the monoclonal antibody of Falini et al., (i.e. Ber-H2 with ricin attached) binding immunospecifically to CD30

inherently is at least 95 % identity to instant SEQ ID NO:2. As for the specific method as recited in claim 19, the product of the antibody of the prior art inherently has the cytotoxic effect no matter what method is employed since the product has ricin. In the absence of evidence to the contrary, the burden is on the applicant to prove that the product being used in the claimed method is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

Claims 1-8 and 67 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Tian et al., Cancer Res. 1995 Nov 15; 55(22): 5335-41 in view of Falini et al., (1995, Blood, vol., 85, pages 1-14).

The claims are interpreted as drawn to method of treating Hodgkin's cancer with a subgenus of anti-CD30 antibodies (claims 1-7 and 67), or a protein (claim 8), in which the subgenus has cytotoxic effect to Hodgkin's disease cell line cells without a conjugation to the antibodies, wherein method further comprises chemotherapy in claims 3, 6, and wherein the antibody is a chimeric antibody in clam 2, conjugated to a cytotoxic agent in claim 4, and s a fusion protein comprising the amino acid sequence of a second protein that is not an antibody in claim 5, wherein claim 7 specifies how the cytotoxic effect is determined, wherein claim 8 specifies that the protein competes binding with AC10 or HeFi-1 for CD30.

Tian et al., teach (1) a new class of anti-CD30 antibody (i.e. M44 and HeFi-1) that binds to the ligand-binding site of CD30); (2) CD30 is expressed in both Hodgkin's disease cells, and also in ALCLs; (3) the new class of anti-CD30 antibody (without conjugation to a cytotoxic agent) shows a significant antitumor effects in vivo model of ALCL expressing CD30; (4) in vitro proliferation assay using about 5,000 cells using ^{3}H-thymidine is a well known protocol used in the art (note page 5336); (5) unconjugated moAbs are attractive because they avoid toxicity associated with toxins and isotopes (note page 534)); (6) in vivo experiments at page 533; (7) the art has been disappointed by the inability of an ant-CD30 antibody (Ber-H2) for treating Hodgkin's disease (the paragraph bridging the right and left columns on page 5340). Furthermore, with regards to the specific culture conditions in the claims, the optimum parameters and/or control, it is well within the level of ordinary skill in the art to adjust optimum well known cell line cell culture conditions for the cytotoxic assay. See In re Kronig, 190 USPQ 425.

Tian et al., do not teach Hodgkin's disease cell line cells or in vivo treatment. However, Falini et al., teach Hodgkin's disease cell line cells and how to evaluate cytotoxic effect of an antibody on the Hodgkin's disease cell line cells had been well known in the Hodgkin's disease treatment art. Note page 9, left column. Falini et al., also teach the similarities between ALCL and Hodgkin's disease (note page 5-7), thus suggesting what would work for Hodgkin's disease might also work for ALCL and vice versa.

Therefore, it would have been obvious to use the new class of anti-CD30 antibody for treating patient with Hodgkin's disease with a reasonable expectation of

success, since Tian et al., teach the connection between Hodgkin's disease and ALCL (i.e., both express CD30 that could be targeted for therapy with an antibody). One of ordinary skill would have been motivated to use the new class of anti-CD30 antibody for treating patients with Hodgkin's disease, since Tian et al, teach the new class of anti-CD antibody showing cytotoxic effect in the absence of the conjugation to a cytotoxic agent, and the advantage of unconjugated moAbs is to avoid toxicity associated with toxins and isotopes, thus lessening suffering of cancer patients going through treatment.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642